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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROARK, JESSICA H	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/027,205	JUNE ET AL.	
	Examin r	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,55,60,75 and 87-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,55,60,75 and 87-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/17/03 is acknowledged.
Claims 2-54, 56-59, 61-74 and 76-86 have been cancelled previously.
Claims 1, 55, 60 and 75 have been amended.
Claims 1, 55, 60, 75 and 87-94 are pending and are under consideration in the instant application.

3. This Office Action will be in response to applicant's arguments, filed 7/17/03.
The rejections of record can be found in the previous Office Action (Paper No. 34).

It is noted that New Grounds of Rejection are set forth herein that were not necessitated by Applicant's amendment. This Office Action is therefore Non-Final.

4. In view of the papers filed 7/17/2003, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding Bruce L. Levine to the inventorship.

5. The amendment filed 7/17/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.

The added material which is not supported by the original disclosure is as follows: in the paragraph at lines 8-20 on page 18, Applicant has requested that the 7th line of the paragraph which discloses "about 1mg to 1mg" be amended to read "about 1 μg to 1 g".

While the error in this case is obvious, the correction is not.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112 first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 55, 60, 75, 87-88 and 91-94 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of downregulating HIV-1 fusion cofactor expression by contacting T cells in vitro or in vivo with a solid phase surface that is a bead comprising an anti-CD28 and an anti-CD3 antibody to produce a T cell more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the bead, does not reasonably provide enablement for the method comprising contacting the T cells with solid phase surfaces other than a bead. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification does not provide a sufficiently enabling description of the instant invention. The scope of the instant claims encompasses in their breadth contacting T cells with any solid phase surface comprising anti-CD28 and an anti-CD3 antibodies. The specification discloses that culture of T cells ex vivo with beads coated with both anti-CD28 and anti-CD3 results in increased resistance of those T cells to infection by M-tropic HIV isolates compared to T cells not cultured with the anti-CD28/anti-CD3 beads (e.g., Examples 3 and 4 on pages 34-36). However, the specification does not provide any working examples in which the anti-CD28 and anti-CD3 antibodies are on a solid phase surface other than a bead.

The state of the art as of the effective filing date of the instant application recognized that not all solid phase surfaces comprising anti-CD28 and anti-CD3 antibodies could be used to contact T cells to make them more resistant to infection my M-tropic HIV isolates. Spina et al. (J. Clin. Invest. 1997; 99:1774-1785) report that when plates were coated with anti-CD28 and anti-CD3 antibodies and used to contact T cells from patients infected with HIV, HIV production was not only detectable, but occurred earlier and at greater levels (see page 1775 "Cell culture and induction of virus replication" and page 1776 at the paragraph bridging columns 1 and 2). Creson et al. (J. Virol. 1999; 73(11):9337-9347) directly compared solid phase surfaces that were plastic dishes versus beads comprising anti-CD28 and anti-CD3 antibodies for their ability to increase T cell resistance to infection by an M-tropic HIV isolate and confirmed the earlier observations that costimulation of patient T cells by anti-CD3 and anti-CD28 antibodies immobilized on plastic dishes was a highly sensitive techniques for recovery of HIV from cells (see entire document, but especially Table 1, comments in the Overview on pages 9337-9338 and the Discussion on pages 9343-9347). Creson et al. did however confirm that when the solid phase surface was a bead, the T cells were more resistant to infection (e.g., Table 1).

Thus although the specification provides a working example of a solid phase surface that is a bead, the skilled artisan recognized at the time the application was filed that results obtained with one type of solid phase surface did not provide a basis for predicting the effect of using a different type of solid phase surface. Notably, not only did another solid phase surface not function in the method recited, but it produced the opposite outcome since more viral p24 was detected. The specification does not appear to provide sufficient guidance as to how to distinguish those solid phase surfaces which would produce an increase in resistance to infection versus those which would decrease resistance to infection. Consequently, it would require undue experimentation of the skilled artisan to practice the instant method as broadly as recited.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, it is unpredictable which solid phase surfaces could be used in the instant method; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

Claim Rejections – 35 U.S.C. §§ 102 and 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. The previous rejection of claims 1, 55, 87-90, 92 and 94 under 35 U.S.C. 102(f) has been obviated by the inclusion of Bruce L. Levine as a co-inventor of the instantly subject matter.

10. In view of the inclusion of Bruce L. Levine as co-inventor, the June Declaration under 37 CFR 1.132, filed 11/12/02, is sufficient to overcome the rejection of claims 1, 55, 87-90, 92 and 94 based upon Levine et al. (Science 272:1939-1942 1996, IDS #CH). Accordingly, the rejections under 35 USC 102 and 103(a) with respect to this reference are obviated.

11. It is noted that only a method in which the anti-CD28 and anti-CD3 antibodies are immobilized on a solid phase surface that is a bead appear to be enabled for the reasons set forth supra. The following rejections are set forth with respect to this enabled embodiment.

12. Claims 1, 55, 60, 75, 87-89, 92 and 94 are rejected under 35 U.S.C. 102(e) as being anticipated by Chang (US Pat. No. 6,129,916, of record, see entire document), as evidenced by Levine et al. (Science 272:1939-1942 1996, IDS #CH).

Applicant's arguments, filed 7/17/03, have been fully considered, but are not found convincing. Applicant's arguments are addressed below in the context of the reiterated rejection of record as applied to the amended claims.

As previously noted, Chang teaches and claims a method of increasing the activation or proliferation of T cells comprising contacting T cells with a microbead coupled with a plurality of binding molecules specific for an antigen on a human T cell (see entire document). Chang teaches that an embodiment of the invention includes using microbeads that comprise a binding molecule that is an antibody to CD3 paired with another binding molecule that is specific for T cells, including an antibody to CD28 (see entire document, especially claims 1-2 and columns 11-12). Chang et al. teach several methods for immobilizing antibodies on solid phase surfaces that are beads, including direct immobilization via a covalent modification (see especially columns 7-8).

Applicant argues that there is no teaching or suggestion in Chang to select the combination of an anti-CD3 and an anti-CD28 antibody, because Chang teaches that other molecules can be used.

However, Chang does teach that one embodiment of the invention utilizes an antibody to CD3 along with an antibody to another molecule expressed on a T cell, and Chang clearly lists that a second antibody specific for CD28 (see especially column 12 at lines 7-11). Applicant is reminded that while a disclosed genus does not always anticipate a claim to a species within the genus, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). In the instant case Chang teaches an embodiment in which an anti-CD3 antibody is used in combination with an antibody to another molecule on the T cell that is CD28. Thus Chang does teach the instantly recited species.

Applicant also argues that Chang does not appreciate that reduction of HIV-1 fusion cofactor expression occurs when T cells are contacted with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies or that this leads to an increase T cell resistance to HIV infection, as recited in the amended claims.

While again acknowledging that Chang did not appreciate that the results of administration of this product would include downregulation of CCR5 expression in the T cell and an increase in resistant to infection by an M-tropic HIV isolate compared to a T cell not contacted; the courts have held that there is no requirement that those of ordinary skill in the art know of the inherent property. See MPEP 2131.01(d) and MPEP 2112 - 2113 for case law on inherency.

It has been previously noted that although downregulation of HIV-1 fusion co-factors including CCR5 is not explicitly demonstrated, the use of *in vivo* methodology equivalent to that disclosed in the specification as-filed for *in vitro* experiments indicates that downregulation of the fusion co-factor CCR5 would be an inherent outcome of these methods, irrespective of whether the contacting step is *in vivo* or *in vitro*.

Levine et al. evidence that resistance of T cells to infection with the M-tropic (CCR5-dependent) HIV-1 strain inherently occurs following contact of T cells with a solid phase surface that is a bead comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro* (see entire document). Downregulation of CCR5 also is inherent (as evidenced by the resistance to infection by M-tropic HIV strains).

Applicant argues that the results are not inherent outcomes of contacting a T cells with a solid phase surface comprising an anti-CD28 and an anti-CD3 antibody because other groups have used solid phase surfaces comprising these antibodies and shown that the effect is to enhance viral replication.

As discussed in detail supra, the Examiner acknowledges that the instantly claimed result of increasing the resistance of T cells to M-tropic infection is an outcome that is dependant upon the type of solid phase surface used. However, the solid phase surface taught by Chang is, as in Applicant's methods, a bead coated with anti-CD28 and anti-CD3 antibodies.

When a claim recites using an old composition or structure (e.g. a solid phase surface that is a bead comprising an anti-CD3 antibody and an anti-CD28 antibody) and the use is directed to a result or property of that composition or structure (downregulation of the HIV-1 fusion co-factor CCR5 and resistance to infection), then the claim is anticipated. See MPEP 2112.02. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant also argues that it the use of the same methodology in vivo in Chang as used by Applicant in vitro does not necessarily mean that the same result would be observed in vivo, pointing to the different in vivo versus in vitro effects of soluble anti-CD3 antibody discussed by Chang.

However, Chang provides evidence that antibody coated beads stimulate T cell proliferation in vivo (e.g., the Example at columns 9-11).

Finally, Applicant again argues that because Chang is directed to *in vivo* applications and only mentions in vitro applications in passing and expresses concerns regarding *in vitro* stimulation of lymphocytes that Chang does not teach or suggest in vitro methods.

As previously noted, while Chang teaches and claims an *in vivo* method, Chang does teach the *in vitro* use of a microbead coupled with a plurality of binding molecules specific for an antigen on a human T cell, wherein the binding molecules are an antibody to CD3 and an antibody to CD28 (e.g., column 5, especially lines 31-37). That the *in vitro* method is discussed in the context of later application *in vivo* does not alter the fact that Chang teaches both *in vitro* and *in vivo* methods. In addition, there is no requirement that a teaching be a preferred embodiment or the "focus" of the whole reference.

Because there still does not appear to be anything in the claim language which distinguishes the claims from the teachings of Chang, the rejection is maintained with respect to the enabled embodiment wherein the solid phase surface is a bead.

13. Claims 1, 55 and 87-90 are rejected under 35 U.S.C. 102(b) as being anticipated by Levine et al. (Int. Immunol. 1995; 7(6):891-904, IDS #CI), as evidenced by Levine et al. (Science 272:1939-1942 1996, IDS #CH).

Applicant's arguments, filed 7/17/03, have been fully considered, but are not found convincing. Applicant's arguments are addressed below in the context of the reiterated rejection of record as applied to the amended claims.

Levine et al. #CI teach a method comprising contacting T cells with a solid phase surface that is a magnetic immunobead comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro* (see entire document, e.g., Table 2 and "Short term T cell cultures" on page 892-893). Both anti-human CD3 and anti-human CD28 antibodies are taught (e.g., page 892 - OKT3 is an anti-human CD3 antibody and 9.3 is an anti-human CD28 antibody, as evidenced by their reactivity with human T cells).

Levine et al. #CH evidence that resistance of T cells to infection with the M-tropic (CCR5-dependent) HIV-1 strain inherently occurs following contact of T cells with a solid phase surface that is a bead comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro* (see entire document). Downregulation of CCR5 also is inherent (as evidenced by the resistance to infection by M-tropic HIV strains).

Applicant argues that evidence has been provided that shows that down-regulation of HIV- fusion cofactors such as CCR5 is not an inherent property of contacting T cells with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody.

As noted supra, the Examiner agrees that not all solid phase surfaces function in the instant methods. However, with respect to the enabled embodiment of a solid phase surface that is a bead, it is noted that there is no difference in the product used in the enabled methods and the product used by Levine et al. #CI.

When a claim recites using an old composition or structure (e.g. a solid phase surface that is a bead comprising an anti-CD3 antibody and an anti-CD28 antibody) and the use is directed to a result or property of that composition or structure (downregulation of the HIV-1 fusion co-factor and resistance to infection), then the claim is anticipated. See MPEP 2112.02. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

It is noted that the CAFC recently held in Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001) that the preamble language in claims is an expression of purpose and intended result, and as such is non-limiting, since the language *does not result in a manipulative difference in the steps of the claims*.

Applicant is reminded that the courts have held that there is no requirement that those of ordinary skill in the art know of the inherent property. See MPEP 2131.01(d) and MPEP 2112 - 2113 for case law on inherency.

14. Claims 1, 55, 87-90 and 92-94 are rejected under 35 U.S.C. 102(e) as being anticipated by June et al. (U.S. Pat. No. 6,352,694, see entire document, of record) as evidenced by Levine et al. (Science 272:1939-1942 1996, IDS #CH).

Applicant's arguments, filed 7/17/03, have been fully considered, but are not found convincing. Applicant's arguments are addressed below in the context of the reiterated rejection of record as applied to the amended claims.

June et al. teach and claim a method comprising activating a population of human T cell to proliferate by contacting the cells in vitro with an anti-human CD3 antibody immobilized on a solid phase surface that is a bead and an anti-human CD28 antibody immobilized on the same bead surface (see entire document, e.g., columns 1-3 "Summary of the Invention" and claims 1-3).

June et al. also teach and claim that the bead can be a magnetic immunobead (e.g., claims 4-5). June et al. teach and claim that the antibodies may be immobilized on the solid phase surface by a covalent modification (e.g., claim 7), by an avidin-biotin complex (e.g., claim 8) or by direct immobilization (e.g., claim 9).

Levine et al. #CH evidence that resistance of T cells to infection with the M-tropic (CCR5-dependent) HIV-1 strain inherently occurs following contact of T cells with a solid phase surface that is a bead comprising an anti-CD3 antibody and an anti-CD28 antibody *in vitro* (see entire document). Downregulation of CCR5 also is inherent (as evidenced by the resistance to infection by M-tropic HIV strains).

In addition, June et al. teach that the T cells may be T cells from an HIV infected patient (see e.g., columns 28-30 and 51-53).

Applicant argues that evidence has been provided that shows that down-regulation of HIV- fusion cofactors such as CCR5 is not an inherent property of contacting T cells with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody.

As noted supra, the Examiner agrees that not all solid phase surfaces function in the instant methods. However, with respect to the enabled embodiment of a solid phase surface that is a bead, it is noted that there is no difference in the product used in the enabled methods and the product used by June et al.

When a claim recites using an old composition or structure (e.g. a solid phase surface that is a bead comprising an anti-CD3 antibody and an anti-CD28 antibody) and the use is directed to a result or property of that composition or structure (downregulation of the HIV-1 fusion co-factor CCR5 and resistance to infection), then the claim is anticipated. See MPEP 2112.02. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant is reminded that the courts have held that there is no requirement that those of ordinary skill in the art know of the inherent property. See MPEP 2131.01(d) and MPEP 2112 -2113 for case law on inherency.

It is again noted that the applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The Declaration under 37 C.F.R. 1.132 by Dr. June, file 7/17/03 and stating that the invention disclosed but not claimed in the reference was derived from the inventor of this application, is acknowledged.

However, the June Declaration under 37 CFR 1.132 filed 7/17/03 is insufficient to overcome the rejection of claims 1, 55, 87-90 and 92-94 based upon June et al. (U.S. Pat. No. 6,352,694, of record) as set forth in the last Office action because the Declaration only addresses the product used in the instantly recited method. Both the instant application and the reference claim a method comprising contacting T cells with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies, including wherein the solid phase surface is a bead (e.g., claims 1 and 4).

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. In view of the New Grounds of Rejection set forth supra, the previous rejection of claims 1, 55, 60, 75, 91 and 93 under 35 U.S.C. 103(a) as being unpatentable over Chang (US Pat. No. 6,129,916, of record) in view of the well-known and art-recognized use of avidin-biotin complexes to couple antibodies to solid phase surfaces, including tissue culture dishes, as evidenced by Shattil (US Pat No. 5,561,047, of record) is withdrawn in favor of the rejection under 35 USC 112, first paragraph.

17. Claims 60, 75, 87-90 and 92-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over June et al. (U.S. Pat. No. 6,352,694, of record) as evidenced by Levine et al. (Science 272:1939-1942 1996, IDS #CH), in view of Chang (U.S. Pat. No. 6,129,916, of record).

Applicant's arguments, filed 7/17/03, have been fully considered, but are not found convincing. It is believed that Applicant's arguments regarding the Chang reference and its teachings, as well as the reasons why the June Declaration under 37 C.F.R. is insufficient to overcome the reference have each been addressed supra and are incorporated herein.

The claims are drawn to *in vivo* methods for downregulating fusion cofactor (CCR5) expression in a T cell by contacting the T cell with a solid phase surface comprising an anti-CD28 and an anti-CD3 antibody, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

June et al. as evidenced by Levine et al. have been discussed supra.

June et al. as evidenced by Levine et al. do not explicitly teach the *in vivo* application of the antibody coated solid surface.

However, Chang has also been discussed supra and Chang does teach that beads comprising anti-CD3 and anti-CD28 can be used for *in vivo* applications.

In addition, June et al. teach that the T cells may be T cells from an HIV infected patient (see e.g., columns 28-30 and 51-53). June et al. note that contacting T cells from an HIV infected patient is useful for increasing the numbers of T cells that can then be returned to the patient, which is therapeutically beneficial to the HIV patient (see especially columns 51-53).

Applicant argues that the in vitro teachings of June et al. do not render obvious the instant claims because the teaching of June et al. that it would be beneficial to increase T cell numbers in an HIV infected patient is entirely different from downregulating HIV-1 fusion co-factors to make the T cells more resistant to M-tropic HIV isolates.

However, the Examiner maintains that one of ordinary skill in the art at the time the invention was made would have found it obvious to apply the method taught by June et al. *in vivo*. Given the teachings of Chang that the same product used by June et al. *in vitro* could also be used *in vivo*, the ordinary artisan would have had a reasonable expectation that the method of June et al. could also be practiced *in vivo*. In view of the teachings of June et al. of the beneficial effect on T cell numbers when T cells are contacted with beads on which anti-CD3 and anti-CD28 have been co-immobilized, the ordinary artisan would have been motivated to administer the beads in vivo; particularly since an in vivo method would obviate potential sources of secondary infection due to ex vivo expansion of the T cells and would reduce the risk of exposure of health care workers to HIV infected cells.

Therefore, the Examiner maintains that the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1, 55, 60, 75, 87-90 and 91-94 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,352,694 (of record) either alone or in combination with Chang (U.S. Pat. No. 6,129,916, of record).

Although the conflicting claims are not identical, they are not patentably distinct from each other because as set forth supra, the claims of U.S. Pat. No. 6,352,694 anticipate instant claims 1, 55, 87-90 and 92-94 because the instant limitations are either explicitly claimed, or are inherent in the method claimed in U.S. Pat. No. 6,352,694.

Regarding instant claims 60 and 75, the application of the method in vivo would be an obvious variation of the method claimed by U.S. Patent No. 6,352,694 in view of the teachings of Chang for in vivo applications of anti-CD3+anti-CD28 beads.

Applicant argues that for the reasons set forth supra with respect to the applicant of the June et al. reference as art under 35 USC 102 and 103(a), claims 1, 55, 60, 75, 87-90 and 91-94 are not unpatentable over claims 1-16 of June et al.

Applicant's arguments have been addressed supra. In particular, it is noted that both the pending and patented claims teach the same method steps and the effect recited in the different preambles must each necessarily occur when the same method steps are used. There does not appear to be any material difference in the instant claims.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
October 31, 2003

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PRIMARY EXAMINER
TECH CENTER 1600
10/31/03